IFW 1635

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In Re Application of: Paz EINAT et al.

Application No.: 10/091,333 Conf. No. 1554

Filed: March 6, 2002

For: HYPOXIA-REGULATED GENES

Art Unit: 1635

Examiner: J.B. Ashen

Washington, D.C.

Atty.'s Docket: EINAT 1.1D

Date: March 28, 2005

THE COMMISSIONER OF PATENTS
U.S. Patent and Trademark Office
Customer Service Window
Randolph Building, Mail Stop Amendment
401 Dulany Street
Alexandria, VA 22314

Sir:

Transmitted herewith is a [X] Response [ ]_____
in the above-identified application.

[ ] Small Entity Status: Applicant(s) claim small entity status. See 37 C.F.R. §1.27.

[XX] No additional fee is required.

[ ] The fee has been calculated as shown below:

	(Col. 1) CLAIMS REMAINING AFTER AMENDMENT		(Col. 2) HIGHEST NO. PREVIOUSLY PAID FOR	(Col. 3) PRESENT EXTRA EQUALS	SMALL ENTITY RATE	SMALL ENTITY ADDITIONAL FEE	OR	OTHER THAN SMALL ENTITY RATE	OTHER THAN SMALL ENTITY ADDITIONAL FEE
TOTAL	* 28	MINUS	** 28	0	x 25	$		x 50	$
INDEP.	* 3	MINUS	*** 3	0	x 100	$		x 200	$
FIRST PRESENTATION OF MULTIPLE DEP. CLAIM					+ 180	$		+ 360	$
					ADDITIONAL FEE TOTAL	$	OR	TOTAL	$ 108.00

* If the entry in Col. 1 is less than the entry in Col. 2, write "0" in Col. 3.

** If the "Highest Number Previously Paid for" IN THIS SPACE is less than 20, write "20" in this space.

*** If the "Highest Number Previously Paid for" IN THIS SPACE is less than 3, write "3" in this space.

The "Highest Number Previously Paid For" (total or independent) is the highest number found from the equivalent box in Col. 1 of a prior amendment of the number of claims originally filed.

[XX] Conditional Petition for Extension of Time

If any extension of time for a response is required, applicant requests that this be considered a petition therefor.

[ ] It is hereby petitioned for an extension of time in accordance with 37 CFR 1.136(a). The appropriate fee required by 37 CFR 1.17 is calculated as shown below:

Small Entity Response Filed Within		Other Than Small Entity Response Filed Within	
[ ] First	- $ 60.00	[ ] First	- $ 120.00
[ ] Second	- $ 225.00	[ ] Second	- $ 450.00
[ ] Third	- $ 510.00	[ ] Third	- $1,020.00
[ ] Fourth	- $ 795.00	[ ] Fourth	- $1,590.00
Month After Time Period Set		Month After Time Period Set	

[ ] Less fees ($_____) already paid for ___ month(s) extension of time on _____.

[ ] Please charge my Deposit Account No. 02-4035 in the amount of $_____.

[ ] Credit Card Payment Form, PTO-2038, is attached, authorizing payment in the amount of $_____.

[ ] A check in the amount of $_____ is attached (check no.).

[XX] The Commissioner is hereby authorized and requested to charge any additional fees which may be required in connection with this application or credit any overpayment to Deposit Account No. 02-4035. This authorization and request is not limited to payment of all fees associated with this communication, including any Extension of Time fee, not covered by check or specific authorization, but is also intended to include all fees for the presentation of extra claims under 37 CFR §1.16 and all patent processing fees under 37 CFR §1.17 throughout the prosecution of the case. This blanket authorization does not include patent issue fees under 37 CFR §1.18.

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Atty. Docket: EINAT=1.1D

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RESPONSE

Honorable Commissioner for Patents
U.S. Patent and Trademark Office
Customer Service Window
Randolph Building, Mail Stop Amendment
401 Dulany Street
Alexandria, VA 22314

Sir:

The present communication is responsive to the official action of December 28, 2004. Claims 12-39 presently appear in this case. Claims 12-16 and 24-39 have been withdrawn from consideration. No claims have been allowed. The official action of December 28, 2004, has now been carefully studied. Reconsideration and allowance are hereby respectfully urged.

Briefly, the present invention relates to an RNA molecule that targets mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:10. The targeting preferably prevents processing, splicing, transport, or translation of

the mRNA, or results in mRNA degradation. The RNA may be an antisense RNA or a ribozyme. The invention further relates to an RNA molecule that targets DNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:10. Preferably, the targeting results in a transcriptionally inactive product. Applicants also consider therapeutic methods of use of such RNA to be part of the present invention.

The examiner has acknowledged applicants' traversal of the restriction requirement, but has maintained it and made it final. The examiner has acknowledged applicant's assertion that certain process claims should be rejoined with the product claims of claims 17-23 if the latter should be found allowable. Applicants continue to traverse this requirement and wish to preserve their rights under 37 C.F.R. §1.144 to petition from this requirement for restriction at an appropriate time, particularly if at least process claims 24-33, 38 and 39, as well as claims 35-37, are not rejoined with the elected claims if the latter are found to be allowable.

The examiner states that applicant has considered the references cited in the IDS filed on March 6, 2002, only in part, because only three of the literature references could be found by the examiner in the prior application files. The examiner has requested that the remainder of the references be submitted in order that they be considered. These additional

references are now again being gathered and are being submitted herewith, or will be submitted shortly thereafter as soon as they are all obtained.

Claims 20 and 22 have been rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. The examiner states that claim 20 is drawn to an RNA molecule that targets mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:10 that is an antisense RNA molecule, and claim 22 is drawn to an RNA molecule that targets DNA encoding a particular polypeptide. The examiner states that he could find support only for RNA molecules that are ribozymes, but no support could be found for new claims to an RNA molecule that is an antisense RNA, or an RNA molecule that targets DNA. This rejection is respectfully traversed.

The examiner's attention is invited to page 23, lines 21-24, of the present specification, which states:

> AS [antisense] oligonucleotide sequences may be short sequences of DNA, typically 15-30 mer, but may be as small as 7 mer (Wagner et al, 1996), designed to complement a target mRNA of interest and form an RNA:AS duplex.

This language provides support for the claim drawn to an RNA molecule that is an antisense RNA. The examiner's attention is invited to page 24, lines 7-10, that states:

> An additional mode of action results from the interaction of AS with genomic DNA to

form a triple helix that may be transcriptionally inactive.

This provides support for an RNA molecule that targets DNA encoding a polypeptide of SEQ ID NO:10. Accordingly, the present specification does contain support for the subject matter of claims 20 and 22. Reconsideration and withdrawal of this rejection are therefore respectfully urged.

Claims 17-20 and 22-23 have been rejected under 35 U.S.C. §102(e) or 35 U.S.C. §103 (a) as being anticipated by or obvious over Chang. The examiner states that Chang discloses an oligonucleotide of SEQ ID NO:15 that is 84.2% identical to the nucleic acid sequence encoding the polypeptide of SEQ ID NO:10, with the 5' end of the 19 nucleobase oligonucleotide of Chang being 100% identical over the first sixteen contiguous nucleobases, to the polypeptide of SEQ ID NO:10 of the instant invention. This rejection is respectfully traversed.

The examiner states that the 5' end of the 19 nucleobase oligonucleotide of Chang is 100% identical over the first sixteen contiguous nucleobases, to the polypeptide of SEQ ID NO:10 of the present invention. This statement is rather confused, as nucleobases cannot correspond to polypeptides. The examiner is apparently referring to SEQ ID NO:2, which is the gene that includes the coding sequence that encodes the polypeptide of SEQ ID NO:10. See page 55, lines

8-10, of the present specification. It is apparent that the portion of SEQ ID NO:2 that is 100% identical to the first sixteen contiguous nucleobases of SEQ ID NO:15 of Chang are those sixteen nucleobases at positions 19-34 of SEQ ID NO:2. These correspond exactly to the first sixteen nucleobases of SEQ ID NO:15 of Chang. However, within SEQ ID NO:2 the coding sequence begins with the ATG at positions 219, 200 and 221. This can readily be determined by comparing the codons beginning with this ATG with the amino acid sequence of SEQ ID NO:10.

Claim 17 requires that the RNA molecule target mRNA encoding a polypeptide having the amino acid sequence of SEQ ID NO:10. The nucleobases at positions 19-34 of SEQ ID NO:2 are upstream of the coding region, and therefore do not encode a polypeptide having the amino acid sequence of SEQ ID NO:10. These nucleobases will not bind an mRNA encoding the polypeptide as they will not appear in the mRNA, which includes only the coding region of the gene. The same is true with respect to claim 22, as the DNA that is targeted by the molecule cited by the examiner does not encode a polypeptide having the amino acid sequence of SEQ ID NO:10. As it does not encode any part of the polypeptide, anything targeting it cannot anticipate. No other nucleotide sequence that would encode the polypeptide of SEQ ID NO:10 would be obvious from

Chang. Accordingly, reconsideration and withdrawal of this rejection are respectfully urged.

Claims 17-20 and 22-23 have been rejected under 35 U.S.C. §102(a) or 35 U.S.C. §103(a) as being anticipated by or obvious over Sutcliffe. The examiner states that Sutcliffe discloses SEQ ID NO:16 that is twenty nucleobases in length, and 100% identical to the nucleic acid sequence encoding the polypeptide of SEQ ID NO:10. This rejection is also respectfully traversed.

The sequence listing of Sutcliffe has only thirteen sequences. Thus, it cannot be determined what sequence the examiner considers to be SEQ ID NO:16. However, in reviewing Sutcliffe, we fortuitously stumbled upon a twenty nucleobase primer at page 71, line 18, which is 100% identical to nucleobases 12-31 of SEQ ID NO:2. If this is the sequence to which the examiner refers, it clearly suffers from the same deficiency as discussed above with respect to Chang. Nucleobases 12-31 of SEQ ID NO:2 do not encode SEQ ID NO:10. They are upstream from the ATG codon that commences the coding the region. Accordingly, as the region of SEQ ID NO:2 that this primer corresponds to is not in the coding region, this primer cannot anticipate or make obvious anything within the scope of claims 17, 22, or those claims dependent therefrom. Reconsideration and withdrawal of this rejection for the same

reasons discussed above in reference to Chang are therefore also respectfully urged.

Claims 17-23 have been rejected under 35 U.S.C. §102(e) or 35 U.S.C. §103(a) as being anticipated by or obvious over Pavco. The examiner states that Pavco discloses an RNA molecule that is a hammerhead ribozyme of SEQ ID NO:7749, the binding arms of which target (with 94.1% complementarity including the first five nucleobases from the 5' and 3' end of each binding arm, thus indicating that sufficient binding for mRNA degradation would occur by complementary binding of each binding arm), the nucleic acid sequence (the mRNA or the coding DNA) encoding the polypeptide of SEQ ID NO:10 of the instant invention. This rejection is also respectfully traversed.

The ribozyme SEQ ID NO:7749 of Pavco has been carefully studied, but applicant has been unable to determine what portion of the sequence encoding the polypeptide of SEQ ID NO:10 corresponds thereto. It would be very helpful if the examiner would specifically refer thereto by nucleotide numbers from SEQ ID NO:2. To the extent that the examiner is referring to the poly-A section at the end of SEQ ID NO:2, this is clearly not part of SEQ ID NO:2 that encodes the polypeptide of SEQ ID NO:10. The last amino acid residue (Cys) of SEQ ID NO:10 is encoded by the TGT at positions 12,

13 and 14 of SEQ ID NO:2. Any nucleobases downstream thereof are not part of the coding sequence. It is requested that the examiner identify the specific nucleobases of SEQ ID NO:2 of the present specification that allegedly correspond to the nucleobases of the binding arms of SEQ ID NO:7749 of Pavco, and show that they are within the portion of the sequence that encode the polypeptide of SEQ ID NO:10. Otherwise, it is requested that this rejection be reconsidered and withdrawn.

The additional prior art made of record and not relied upon has been noted, as has the examiner's implicit recognition that it is insufficiently pertinent to warrant its application against the claims.

It is submitted that all of the claims now present in the case clearly define over the references of record and fully comply with 35 U.S.C. §112. Reconsideration and allowance are therefore earnestly solicited.

Respectfully submitted,

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